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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,386	12/13/2005	Hidekazu Inoue	58778.000005	8779

21967 7590 11/13/2006

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EXAMINER
MOORE, SUSANNA

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/560,386	INOUE ET AL.	
	Examiner	Art Unit	
	Susanna Moore	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *25 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicant's arguments filed September 25, 2006 have been fully considered. All the Objections to the Specification and Claims have been withdrawn.

Claim Rejections - 35 USC § 112

The enablement rejections of the R5 and R6 variables and the solvates are withdrawn as a result of Applicant's Remarks and amendments.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 9, the term "PDE7" renders the claim indefinite because it is unclear what Applicant regards as the invention. "PDE7" is found in various isoforms and there is no PDE7 per se. Does Applicant intend all or just some, and in the latter case, which one(s)?

Applicant recites the Specification provides "sufficient structural and functional parameters to adequately define PDE7 as encompassing each of the PDE7 isoforms," but no where in the Specification is there any mention of the different PDE7 isoforms. There are two genes that encode PDE7A and PDE7B. See Lugnier (Pharma & Therap.(2006) page 378, section 3.7. The Specification does not provide any specific indication that Applicants intended all isoforms. For example, in the assay it is impossible to tell which isoform was actually used.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. The instant claim embraces hundreds of thousands of compounds with a substituted phenyl or pyridyl pyrazolopyrimidinone scaffold with a variety of substituents at four positions. These variations to the pyrazolopyrimidinone scaffold give a diverse range of compounds, which provide different physical and chemical properties to the individual substituted pyrazolopyrimidinone framework.

(b) Scope of the diseases covered. Claims 1-9 are drawn to compounds and compositions thereof as PDE7 inhibitors. The Scope is unknown because there is no standard list of diseases, which cause or are caused by an inhibition of PDE7.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: That provided is very limited. The dosage range information, 0.1 to 100 mg, is broad. Moreover, this is generic, the same for the many disorders covered by the Specification and all PDE7 isoforms. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for all diseases or conditions, which cause or are caused by the inhibition of PDE7.

(D) State of the Prior Art: These compounds are substituted phenyl or pyridyl pyrazolopyrimidinone compounds. So far as the examiner is aware, no substituted phenyl or pyridyl pyrazolopyrimidinone compounds of any kind have been used for the treatment of any or all inflammatory diseases and immunological diseases nor is there any useful inhibition of these isoforms per se. Their potential remains at the level of speculation. As of the filing date, there are no references, which provide firm evidence that inhibition per se of PDE7 isoforms is of any

established use. The Specification does not provide any specific indication that Applicants intended all isoforms. For example, in the assay it is impossible to tell which isoform was actually used.

(E) Working Examples: The Applicant has not provided any working examples to any utility. Applicant presents summarized data for approximately 200 compounds as inhibition of an unspecified PDE7 isoform on page 52-56 of the Specification. Moreover, of the different isoforms currently known for PDE7, i.e. PDEA1, PDEA2, PDEA3 and PDEB, the inhibition assays do not discriminate as to which isoform, if any one, was used for the assay. The Specification provides two inhibition assays PDE7 and PDE4, on pages 20-23.

(F) Skill of those in the art: The claim(s) contains subject matter which was not described in the Specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled. Applicant has not provided any evidence to the contrary. Applicant cites the Castro et. al. reference, "PDE7 has the potential to regulate human T cell functions including cytokine production, proliferation and expression of activation markers. However, its specific role in T cell function is still unclear since a *selective PDE7 inhibitor had not been established* (emphasis added) Castro at 232." The words "potential" and "unclear" provide the state of the prior art as of 2005, which was still very speculative and unknown territory.

(G) The quantity of experimentation needed: Owing especially to factors A, C and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Applicant states, "These PDE7 inhibiting compounds suppress T-cell activation" but provide no evidence of this utility. Just merely reciting a utility is not sufficient to overcome an enablement rejection. The Examiner suggests providing a Declaration similar to the one provided for co-pending Application 10866198, wherein a pharmacology assay was completed which showed the suppression of T-cell activation.

Claim Rejections - 35 USC § 103

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bunnage et. al. (U.S. 6,677,335 and U.S. 6,407,114).

A prior art reference does not have to teach the same utility. The fact that the prior art compounds are not disclosed to have this property is not enough to avoid an obviousness rejection. Applicants must show that the prior art compounds do not actually have the property

disclosed here, by suitable comparative testing. Cf *In re Dillon*, 16 USPQ2nd 1897, 1901; *In re Hoch*, 166 USPQ 406; *Brown v. Gottshalk*, 179 USPQ 65; *In re Murch*, 175 USPQ 430. Note also *In re Lintner*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). It is not necessary for the prior art to have recognition or appreciation of this activity for other than method of use claims. See also *In re Shetty*, 195 USPQ 753 for a case where the prior art did not teach applicants' exact utility. Note also *In re Baxter Travenol Labs,* 21 USPQ2d 1281, 1285 which states, "Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." Note also *In re Ona*, 38 USPQ2d 1597 ("...all benefits need not be explicitly disclosed to render the claims unpatentable..."). That is, mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention, *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA1979) "The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." *Ex parte Obiaya*, 227 USPQ 58, 60 (Board held asserted advantage would flow naturally from following the suggestion of the prior art.). See also *Lantech Inc. v. Kaufman Co. of Ohio Inc.*, 12 USPQ2d 1076, 1077 (Fed. Cir. 1989), cert. denied, 493 U.S. 1058 (1990) (unpublished - not citable as precedent) ("The recitation of an additional advantage associated with doing what the prior art suggests does not lend patentability to an otherwise unpatentable invention."). See MPEP 2144 and 2145.

Applicants recite, "Furthermore, the '335 patent does not teach or suggest modifying the compounds disclosed there in any manner to make them PDE7 selective," (page 9, third full

paragraph). Applicant is not claiming a selective PDE7 inhibitor in claim 9, only a PDE7 inhibitor.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims in copending case 10866198. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims are also embraced in copending case 10866198.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The compounds in the present case represented by formula (IA) and (IB) form positional isomers of the compounds in copending case 10866,198 represented by formula (IA) and (IB), wherein A=N. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify for reasons set forth above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SM

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